

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re: Cagle, et al.

Serial No. 10/715,055

Confirmation No. 3314

Filed: November 17, 2003

Group Art Unit: 1618

Examiner: Z. Fay

For: "Method of Treating Ophthalmic Infections with Moxifloxacin Compositions"

**DECLARATION UNDER 37 CFR §1.132**

Customer Service Window  
Randolph Building  
401 Dulany Street  
Alexandria, VA 22314

Dear Sir:

I, Geoffrey R. Owen, hereby say and declare as follows.

1. I received my bachelor's degree in the Natural Science Tripos from Cambridge University, England, in 1968. I received my doctorate degree in organic chemistry from Cambridge University in 1971. Since 1994, I have worked at Alcon Laboratories, Inc. or Alcon Research, Ltd. (collectively "Alcon"), where I have held various positions in the Optical Research, Consumer Products Research, and Pharmaceutical Research Groups.

2. My title at Alcon is Technical Director, Pharmaceutical Research, a position I have held since 2000. My responsibilities include designing, preparing, and testing topical ophthalmic pharmaceutical formulations. Pharmacokinetic studies of topical ophthalmic products and product candidates are a routine part of my job responsibilities in the Pharmaceutical Research Group, and I have extensive

experience designing, preparing, conducting and analyzing studies of fluoroquinolone antibiotic compounds. Since 2000, I have published 11 articles relating to ocular pharmacokinetics of topical ophthalmic drug products, 8 of which relate to fluoroquinolones. My experience with ophthalmic formulations in general has been continuous since 1990.

3. I am aware that U.S. Patent Application No. 10/715,055 (the Application) is directed, in part, to methods of treating ophthalmic infections via topical administration of compositions containing moxifloxacin at a concentration of 0.1 to 1.0 wt. %.

4. I have reviewed the Declaration of Dr. David Stroman dated May 22, 2007 ("Dr. Stroman's Declaration"), and understand that it has been considered by the U.S. Patent and Trademark Office ("USPTO") in connection with the examination of the Application. I also understand that the Examiner reviewing the Application on behalf of the USPTO has requested that the Applicants provide additional data to support their contention that moxifloxacin compositions exhibit superior ocular penetration properties over the entire concentration range recited in the Application's claims (i.e., 0.1 to 1.0 wt. %).

5. Ocular penetration studies are routinely conducted using an *ex vivo* corneal penetration model that was described by Schoenwald and Huang in an article published in the Journal of Pharmaceutical Sciences in 1983. This article is cited in Dr. Stroman's Declaration in Paragraph 18, and is attached to Dr. Stroman's Declaration as Appendix F. This corneal penetration model ("the Steady-State Model"), which uses a corneal perfusion chamber and rabbit cornea, is well accepted as an accurate and reliable representation of ocular penetration *in vivo*. The Schoenwald, et al. article has been cited more than 200 times in the scientific literature.

6. All of the testing presented in this paragraph and the remainder of this Declaration was performed by me or under my direction. Formulations of various fluoroquinolone compounds were prepared by adding to a buffered saline solution having a physiological pH (pH = 7.3) an amount of fluoroquinolone equivalent to 0.1 mmol (~ 0.004 wt. %)<sup>1</sup>. These formulations were then tested using the Steady-State Model to investigate their corneal penetration properties. The results are shown in Table 1 and Figure 1 below.

**TABLE 1**

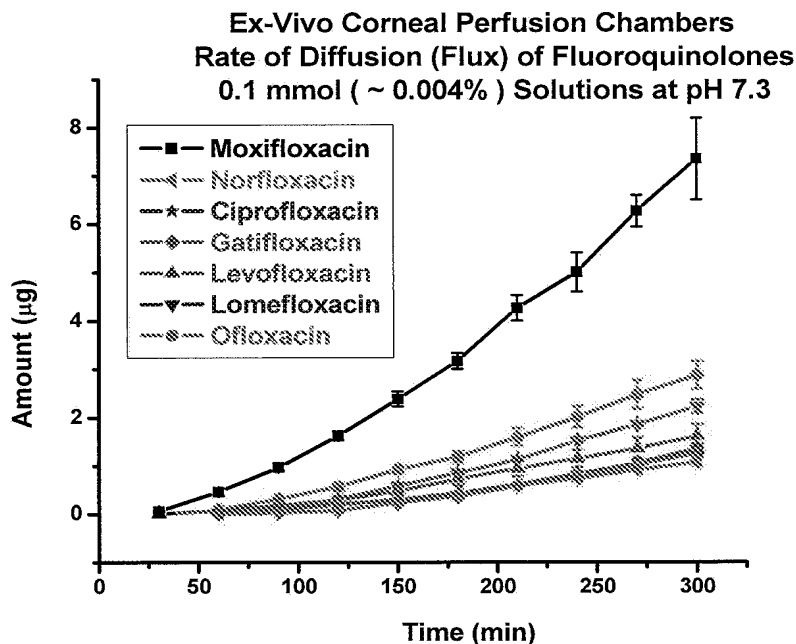
**Ex-Vivo Corneal Perfusion Chambers  
 Fluoroquinolone Comparison  
 0.1 mmol (~0.004%) Solutions at pH 7.3**

Fluoroquinolone	No. of eyes	Rate ( $\times 10^{-2}$ $\mu\text{g}/\text{min}$ )	300 minute Accumulation ( $\mu\text{g}$ )	Lag Time (min)	Permeability Coefficient * ( $\times 10^{-7}$ cm/sec)
Moxifloxacin	3	$2.9 \pm 0.3$	$7.0 \pm 0.5$	$59 \pm 6$	$111 \pm 10$
Ofloxacin	4	$1.2 \pm 0.1$	$2.8 \pm 0.3$	$74 \pm 2$	$53 \pm 5$
Lomefloxacin	3	$1.0 \pm 0.02$	$2.2 \pm 0.1$	$91 \pm 3$	$45 \pm 1$
Levofloxacin	3	$0.70 \pm 0.09$	$1.6 \pm 0.2$	$76 \pm 10$	$30 \pm 4$
Gatifloxacin	3	$0.65 \pm 0.04$	$1.2 \pm 0.1$	$115 \pm 4$	$27 \pm 2$
Ciprofloxacin	5	$0.55 \pm 0.07$	$1.1 \pm 0.1$	$84 \pm 12$	$25 \pm 3$
Norfloxacin	3	$0.48 \pm 0.02$	$1.0 \pm 0.1$	$82 \pm 7$	$23 \pm 1$

\* These values were calculated using the original concentrations of the fluoroquinolones in the donor (epithelial) chamber.

<sup>1</sup> All of the testing presented in this Declaration compared formulations containing equivalent concentrations of the respective fluoroquinolones.

**FIGURE 1**



7. The data in Table 1 and Figure 1 show a rank order of ocular penetration, with moxifloxacin solution being superior to all of the others. These results, which were generated in approximately 2003, have been published, in part (i.e., the data relating to moxifloxacin and gatifloxacin), in the following two publications: the series of articles published as a Special Supplement to the November 2005 edition of Survey of Ophthalmology, International Review Journal (volume 50, supplement 1) and the abstract published as "Corneal penetration and changes in corneal permeability of moxifloxacin versus gatifloxacin" in Invest. Ophthalmol. Vis. Sci. 2004 45: E-Abstract 4910. A copy of the Survey of Ophthalmology publication was attached to Dr. Stroman's Declaration as Appendix E. A copy of the Invest. Ophthalmol. Vis. Sci. publication is attached to the present Declaration as Appendix A.

8. The Steady-State Model is predictive of the relative ocular penetration properties of drug compositions tested at identical concentrations, and this is true

regardless of the drug concentration used in the test. Nevertheless, I understand that the Examiner reviewing the Application has requested comparisons of moxifloxacin compositions to other fluoroquinolone compositions at drug concentrations greater than 0.5 wt.%. In response to that request, I performed additional tests at drug concentrations of 0.1, 0.3, 0.5, 0.75 and 1.0 wt. %, as described below.

9. Ideally, topical ophthalmic formulations have a pH as close to physiological pH (~pH 7.3) as possible. However, some drugs are not sufficiently soluble at that pH to permit comparative testing at identical drug concentrations. In those cases, it is necessary to reduce the pH for the insufficiently soluble fluoroquinolone to a point where the desired drug concentration can be achieved. The Steady-State Model was used to generate comparative corneal penetration data for the indicated fluoroquinolones at drug concentrations of 0.1, 0.3, 0.5, 0.75 and 1.0 wt.%, and the results are shown in Tables 2A, 2B, 2C, 2D, and 2E, respectively.<sup>2</sup> The results are also presented in graphical form in Figures 2A, 2B, 2C, 2D, and 2E, respectively. These results clearly demonstrate the significantly superior corneal penetration properties exhibited by moxifloxacin compositions over compositions containing the other tested fluoroquinolones.

<sup>2</sup> All fluoroquinolones were tested in buffered saline solution (pH = 7.3) unless the desired drug concentration could not be obtained. In some cases, a target concentration of a given fluoroquinolone could not be reached without damaging the cornea used in the Steady-State Model because the solution pH would have had to be adjusted to a pH that was too acidic to permit the rabbit cornea to survive. Even though it involved a less than ideal pH, a comparison of compositions containing moxifloxacin to ofloxacin and levofloxacin was also performed at a fixed pH of 5.8 and at drug concentrations of 0.3, 0.5 and 0.75 wt.%. Moxifloxacin was not sufficiently soluble at pH 5.8 to obtain a 1.0 wt.% composition so no comparative test at 1.0 wt.% was conducted at pH 5.8. The results are shown in Tables B1 – B3, attached in Appendix B.

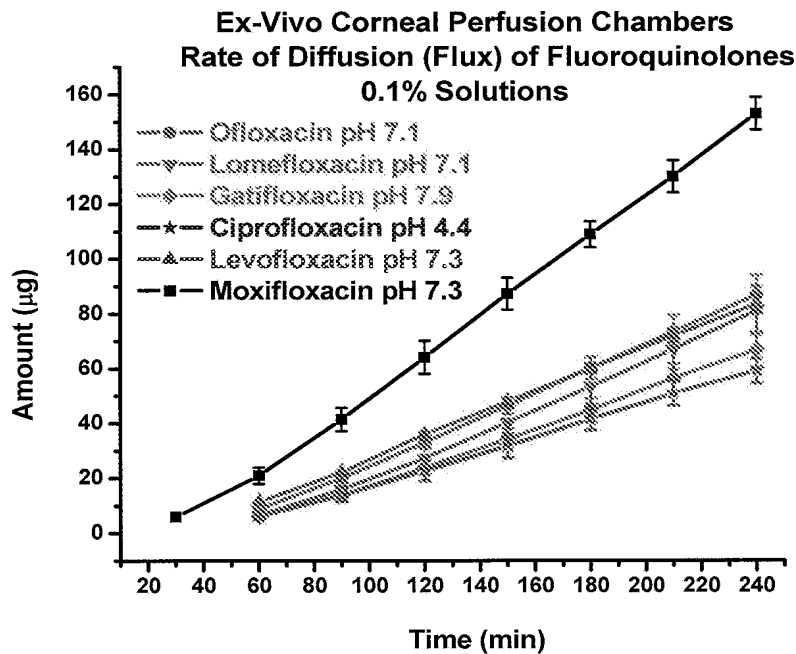
**TABLE 2A**

**Ex-Vivo Corneal Perfusion Chambers  
Fluoroquinolone Comparison  
0.1% Solutions**

Fluoroquinolone	pH	Rate ( $\mu\text{g}/\text{min}$ )	240 minute Accumulation ( $\mu\text{g}$ )	Lag Time (min)	Permeability Coefficient ( $\times 10^{-7}$ cm/sec)
Moxifloxacin	7.3	0.74	158	25	112.9
		0.72	147	37	110.9
Ofloxacin	7.1	0.47	93.2	43	72.4
		0.4	79.8	41	61.6
Levofloxacin	7.3	0.42	87	33	64.3
		0.39	81	31	59.4
Lomefloxacin	7.1	0.46	88.3	48	70.7
		0.38	70.7	52	57.7
Gatifloxacin*	7.9	0.31	59.8	48	47.8
		0.37	72.3	46	57.2
Ciprofloxacin	4.4	0.28	67.8	48	43.4
		0.32	68.4	36	48.4

\* Gatifloxacin was added to the buffered saline solution (pH 7.3) as a free base and caused the pH to increase.

**Figure 2A**

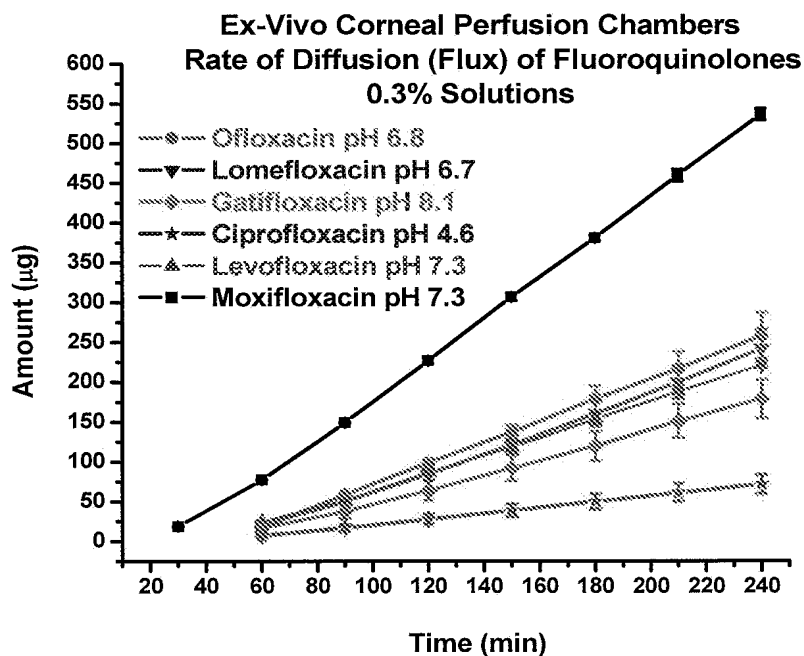


**TABLE 2B**

**Ex-Vivo Corneal Perfusion Chambers  
 Fluoroquinolone Comparison  
 0.3% Solutions**

Fluoroquinolone	pH	Rate ( $\mu\text{g}/\text{min}$ )	240 minute Accumulation ( $\mu\text{g}$ )	Lag Time (min)	Permeability Coefficient ( $\times 10^{-7} \text{ cm}/\text{sec}$ )
Moxifloxacin	7.3	2.5	524	27	125.7
		2.5	540	28	130.1
Ofloxacin	6.8	1.1	231	39	58.6
		1.5	287	52	77.8
Lomefloxacin	6.7	1.4	261	48	69.6
		1.1	213	48	56.8
Levofloxacin	7.3	1.1	226	39	57.5
		1.1	215	43	55.9
Gatifloxacin	8.1	0.81	192	52	41.4
		1	202	42	52
Ciprofloxacin	4.6	0.30	59.3	45	15.6
		0.42	84.9	38	21.5

**FIGURE 2B**

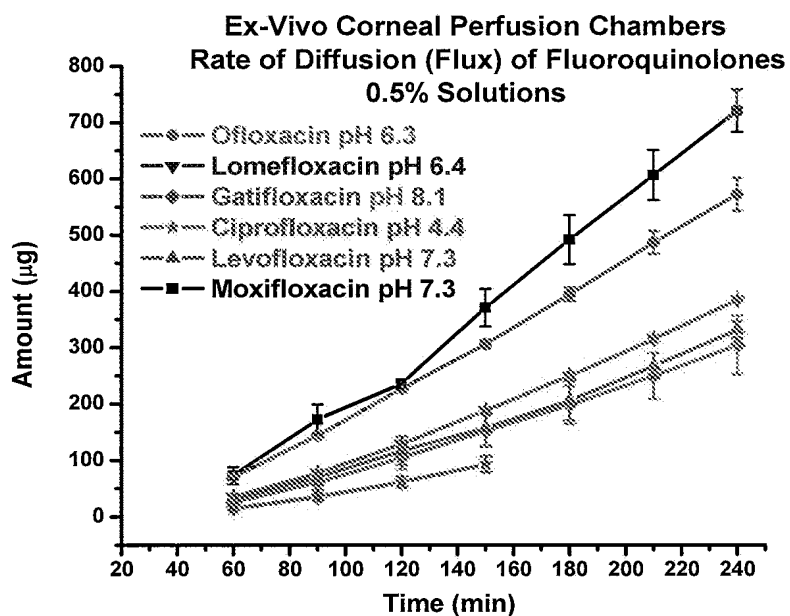


**TABLE 2C**

**Ex-Vivo Corneal Perfusion Chambers  
Fluoroquinolone Comparison  
0.5% Solutions**

Fluoroquinolone	pH	Rate ( $\mu\text{g}/\text{min}$ )	240 minute Accumulation ( $\mu\text{g}$ )	Lag Time (min)	Permeability Coefficient ( $\times 10^{-7}$ cm/sec)
Moxifloxacin	7.3	3.7	758	38	114.7
		3.5	666	49	106.6
Ofloxacin	6.3	2.6	543	35	81.1
		3	593	40	90.8
Lomefloxacin	6.4	1.97	380	47	60.3
		1.95	369	51	59.7
Levofloxacin	7.3	1.7	344	38	52.2
		1.6	292	56	48.7
Gatifloxacin	8.1	1.8	347	47	55
		1.3	247	51	40.1
Ciprofloxacin	4.4	0.98	193	43	30.1
		0.76	146	47	23.2

**FIGURE 2C**



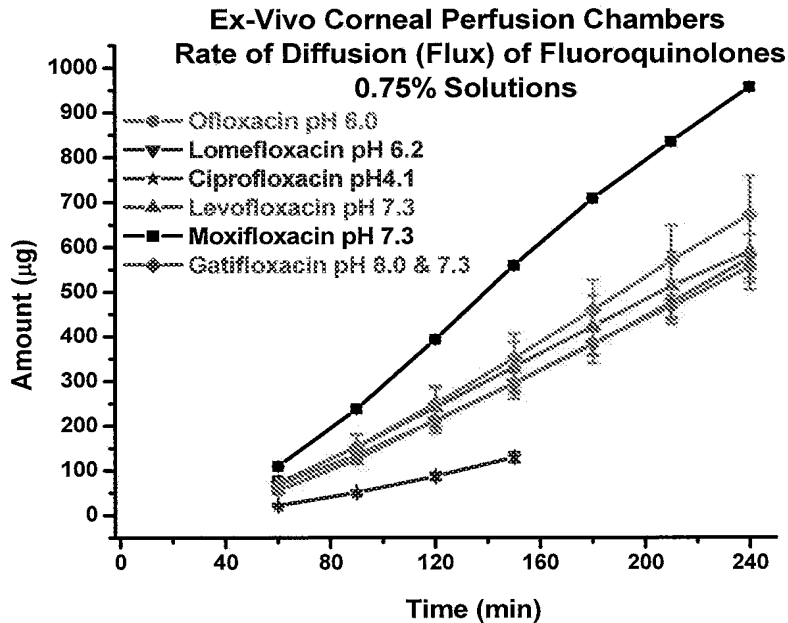


**TABLE 2D**  
**Ex-Vivo Corneal Perfusion Chambers**  
**Fluoroquinolone Comparison**  
**0.75% Solutions**

Fluoroquinolone	pH	Rate (µg/min)	240 minute Accumulation (µg)	Lag Time (min)	Permeability Coefficient ( $\times 10^{-7}$ cm/sec)
Moxifloxacin	7.3	4.8	973	36	97.6
		4.9	981	39	99.5
Gatifloxacin*	8	3.3	432	53	87.2
		4.4	868	44	90.5
	7.3	3.3	650	43	67.5
		3.5	714	35	71.3
Levofloxacin	7.3	3.3	683	33	68
		2.5	508	38	51.7
Lomefloxacin	6.2	3.1	616	39	62.5
		2.6	506	45	52.9
Ofloxacin	8	2.5	478	51	51.9
		2.8	549	47	58
	6.9	2.8	564	38	58.3
		3.1	620	38	62.7
Ciprofloxacin	4.1	1.3	255	43	26.8
		1.1	216	44	22.5

\*As in the other tests, gatifloxacin was added to the buffered saline solution (pH 7.3) as a free base and caused the pH to increase. In a second sample of the gatifloxacin solution, the pH was adjusted back to pH 7.3.

**FIGURE 2D**

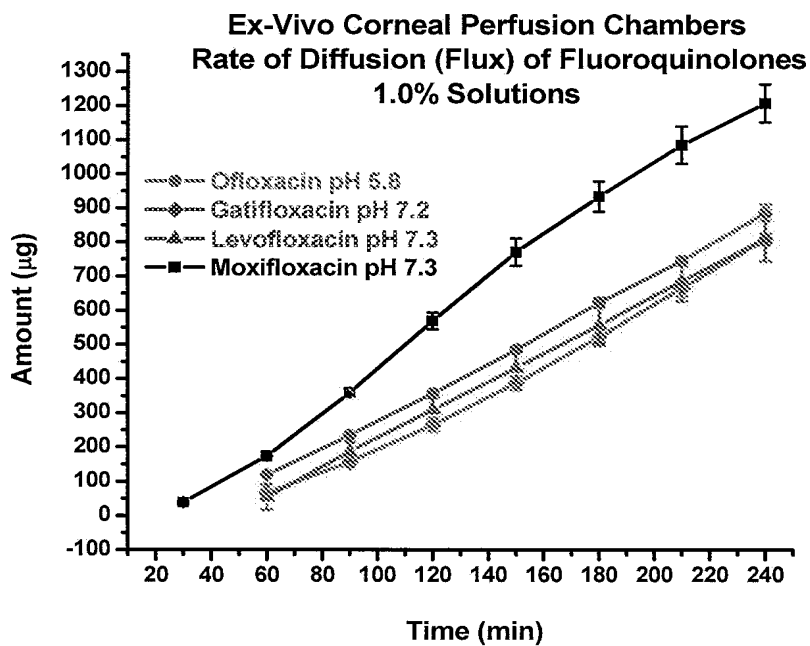


**TABLE 2E**

**Ex-Vivo Corneal Perfusion Chambers  
 Fluoroquinolone Comparison  
 1.0% Solutions**

Fluoroquinolone	pH	Rate ( $\mu\text{g}/\text{min}$ )	240 minute Accumulation ( $\mu\text{g}$ )	Lag Time (min)	Permeability Coefficient ( $\times 10^{-7} \text{ cm}/\text{sec}$ )
Moxifloxacin	7.3	5.5	1191	24	84.3
		6.1	1314	26	94.1
Ofloxacin	5.8	4.1	858	33	63.5
		4.4	899	35	67.4
Levofloxacin	7.3	4	748	52	61
		4.4	875	40	67.1
Gatifloxacin	7.2	4.2	809	48	64.6
		4.1	763	54	62.9

**FIGURE 2E**



10. The data in Tables 2A – 2E and Figures 2A – 2E show the significantly superior corneal penetration property of moxifloxacin compositions compared to the other tested fluoroquinolones. The superior results for moxifloxacin compositions are consistent across all of the tested drug concentrations tested (0.1, 0.3, 0.5, 0.75 and 1.0 wt.%).

11. I also compared the ocular penetration properties of moxifloxacin and ofloxacin compositions in the *in vivo* rabbit model described in “A novel *in vivo* model that mimics human dosing to determine the distribution of antibiotics in ocular tissues,” Journal of Ocular Pharmacology and Therapeutics, 23(4), 335-342 (2007). The tested compositions contained 0.5, 0.75 and 1.0 wt.% of each fluoroquinolone.<sup>3</sup> The results are shown in Tables 3A – 3C.

**TABLE 3A**  
 0.5 % Drug Concentration  
 Ocular Distribution of Fluoroquinolones  
 1 Hour after a Single Topical Dose

	Moxifloxacin 0.5% @ pH 7.3	Ofloxacin 0.5% @ pH 6.3	Ratio Moxi / Oflox
Tissue	Concentration ( µg/g or µg/mL ) Mean ± SE (n = 4)		
Aqueous Humor	2.6 ± 0.5	1.2 ± 0.2	2.1
Iris-Ciliary Body	1.7 ± 0.5	1.0 ± 0.2	1.7
Cornea	12.5 ± 2.6	7.6 ± 0.8	1.6
Upper Palpebral Conjunctiva	1.5 ± 0.5	0.5 ± 0.1	2.7
Lower Palpebral Conjunctiva	2.0 ± 1.0	0.7 ± 0.1	2.8
Bulbar Conjunctiva	1.6 ± 0.6	1.2 ± 0.2	1.3
Sclera	1.5 ± 0.3	1.2 ± 0.3	1.2

<sup>3</sup> Because ofloxacin was not sufficiently soluble at pH 7.3, the pH of the ofloxacin composition was adjusted to permit the target drug concentration to be soluble. I also evaluated the same two fluoroquinolones at 0.5 and 0.75 wt.% in solutions having a pH of 5.8 even though the target pH for topical ocular products is physiological pH. Moxifloxacin was not sufficiently soluble at pH 5.8 to obtain a 1.0 wt.% solution. The results are shown in Table B4, attached in Appendix B. Even at this less than ideal pH (pH 5.8), superior aqueous humor concentrations of moxifloxacin were achieved. Of the sites or tissues examined in this experiment, aqueous humor drug levels provide the best indication of a drug's ability to penetrate the cornea.

**TABLE 3B**  
 0.75 % Drug Concentration

**Ocular Distribution of Fluoroquinolones  
 1 Hour after a Single Topical Dose**

	<b>Moxifloxacin</b> 0.75% @ pH 7.3	<b>Ofloxacin</b> 0.75% @ pH 6.0	<b>Ratio</b>
<b>Tissue</b>	<b>Concentration ( µg/g or µg/mL )</b> Mean ± SE (n = 4)		<b>Moxi / Oflox</b>
Aqueous Humor	<b>2.5 ± 0.2</b>	<b>1.1 ± 0.2</b>	<b>2.3</b>
Iris-Ciliary Body	<b>1.3 ± 0.3</b>	<b>0.7 ± 0.1</b>	<b>2.0</b>
Cornea	<b>10.3 ± 1.9</b>	<b>6.3 ± 1.0</b>	<b>1.6</b>
Upper Palpebral Conjunctiva	<b>0.5 ± 0.2</b>	<b>0.4 ± 0.1</b>	<b>1.4</b>
Lower Palpebral Conjunctiva	<b>1.8 ± 0.3</b>	<b>0.7 ± 0.2</b>	<b>2.7</b>
Bulbar Conjunctiva	<b>4.9 ± 2.7</b>	<b>0.9 ± 0.2</b>	<b>5.2</b>
Sclera	<b>1.0 ± 0.7</b>	<b>1.0 ± 0.4</b>	<b>1.0</b>

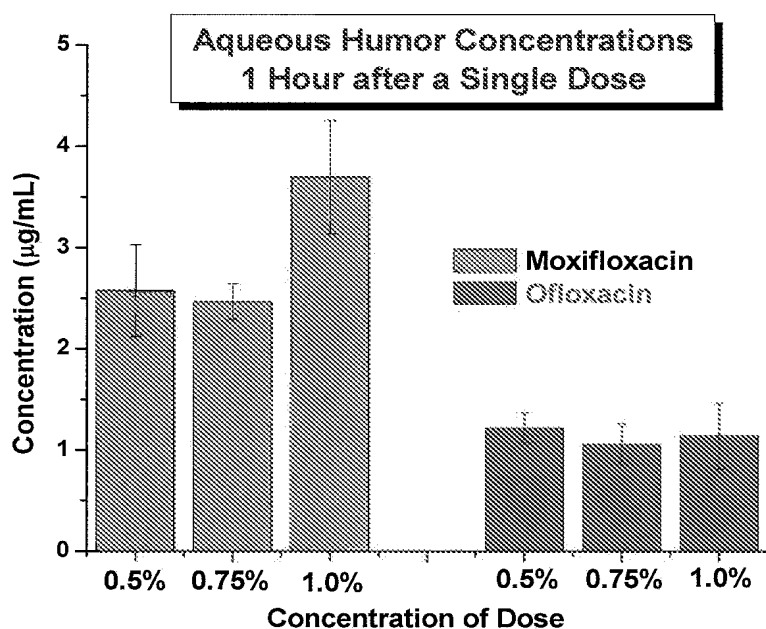
**TABLE 3C**  
 1.0 % Drug Concentration

**Ocular Distribution of Fluoroquinolones  
 1 Hour after a Single Topical Dose**

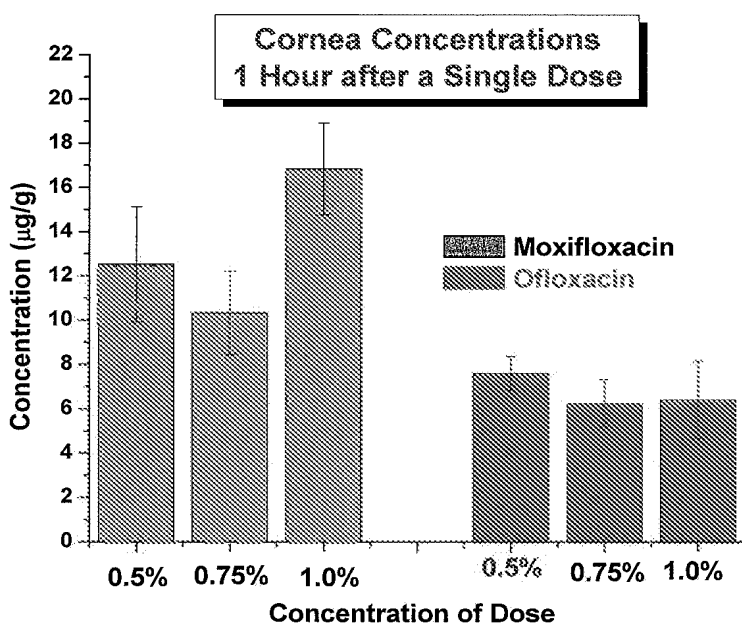
	<b>Moxifloxacin</b> 1.0% @ pH 7.3 (n = 8)	<b>Ofloxacin</b> 1.0% @ pH 5.8 (n = 3)	<b>Ratio</b>
<b>Tissue</b>	<b>Concentration ( µg/g or µg/mL )</b> Mean ± SE		<b>Moxi / Oflox</b>
Aqueous Humor	<b>3.7 ± 0.6</b>	<b>1.1 ± 0.3</b>	<b>3.2</b>
Iris-Ciliary Body	<b>2.0 ± 0.2</b>	<b>0.38 ± 0.2</b>	<b>3.3</b>
Cornea	<b>16.8 ± 2.1</b>	<b>6.4 ± 1.8</b>	<b>2.6</b>
Upper Palpebral Conjunctiva	<b>2.0 ± 0.3</b>	<b>0.6 ± 0.1</b>	<b>3.5</b>
Lower Palpebral Conjunctiva	<b>2.7 ± 0.4</b>	<b>0.6 ± 0.2</b>	<b>4.7</b>
Bulbar Conjunctiva	<b>2.4 ± 0.5</b>	<b>1.2 ± 0.2</b>	<b>2.0</b>
Sclera	<b>3.3 ± 0.6</b>	<b>1.6 ± 0.4</b>	<b>2.1</b>

Figures 3A – 3C depict in bar graph form the results across all three tested drug concentrations for the aqueous humor, cornea, and lower palpebral conjunctiva, respectively.

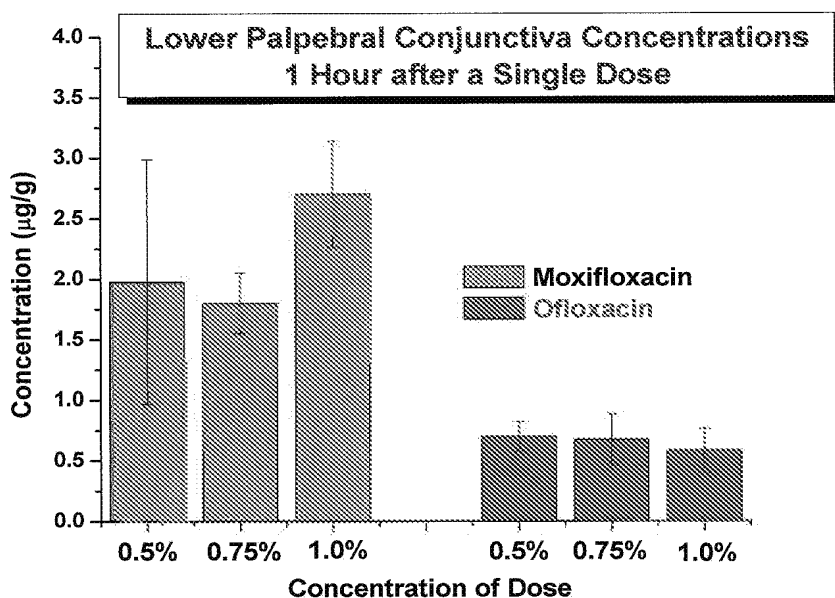
**FIGURE 3A**



**FIGURE 3B**



**FIGURE 3C**



12. The *in vivo* results shown in Tables 3A – 3C and Figures 3A – 3C are consistent with the *ex vivo* Steady-State Model results. At all three drug concentrations (0.5, 0.75 and 1.0 wt.%), moxifloxacin compositions exhibited significantly superior ocular penetration properties compared to ofloxacin compositions.

13. I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine, imprisonment, or both under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing therefrom.

Geoffrey R. Owen  
Geoffrey R. Owen, Ph.D.

Date: February 27<sup>th</sup>, 2008

## Appendix A

Invest. Ophthalmol. Vis. Sci. 2004 45: E-Abstract 4910.

# Corneal Penetration and Changes in Corneal Permeability of Moxifloxacin versus Gatifloxacin

G.R. Owen, O. Dembinska, K.R. Stout and M.K. Mendiola

Alcon Research Ltd, Fort Worth, TX

**Commercial Relationships:** G.R. Owen, Alcon Laboratories, Inc. E; O. Dembinska, Alcon Laboratories, Inc. E; K.R. Stout, Alcon Laboratories, Inc. E; M.K. Mendiola, Alcon Laboratories, Inc. E.

### Abstract

**Purpose:** To compare the effects upon the cornea of moxifloxacin versus gatifloxacin by determining their corneal penetration and change in corneal epithelial permeability following exposure to fluoroquinolone solutions in ex vivo corneal perfusion models. **Methods:** The penetration studies were conducted with solutions of the fluoroquinolones (0.1mM), and the permeability studies were conducted with the commercial preparations: Vigamox™ (0.5% moxifloxacin, Alcon Laboratories, Inc.) which does not contain BAC, and Zymar™ (0.3% gatifloxacin, Allergan, Inc.) which contains 0.005% BAC. In both sets of evaluations, corneas of NZW rabbits were excised and mounted in corneal perfusion chambers according to established methods. The penetration studies were conducted with the fluoroquinolone solutions applied to the epithelial side of the cornea. The rates of accumulation of the fluoroquinolones on the endothelial side of the chamber were determined using HPLC analysis of the perfusates over 5 hours. In the permeability studies, the commercial preparations were applied to the epithelial surface for 5 min. After rinsing, corneas were exposed to carboxyfluorescein (CF) for 5 min and the perfusate collected over 2 hrs. The level of CF in the perfusate was measured by spectrophotometry. **Results:** Moxifloxacin was found to have an apparent corneal permeability coefficient of  $91 \times 10^{-7}$  cm/sec, compared to  $25 \times 10^{-7}$  cm/sec for gatifloxacin. The lag time for the appearance of moxifloxacin on the endothelial side of the cornea was 49 min compared to 99 minutes for gatifloxacin. However, permeability of the cornea to CF was 2.1 pMol/ml/min for Vigamox™ versus 3.4 pMol/ml/min for Zymar™, with peaks of accumulation of 37 pMol/ml for Vigamox™ versus 60 pMol/ml for Zymar™. **Conclusions:** The apparent corneal penetration coefficient of moxifloxacin is 3.6 x greater than gatifloxacin and its appearance on the endothelial side is 2 x faster than gatifloxacin in the absence of any penetration enhancers such as BAC. Although the drug penetration is greater, the corneal permeability to CF is 1.6 x lower after exposure to Vigamox™ compared to Zymar™, illustrating that Vigamox™ maintains better corneal integrity. This demonstrates that the superior corneal penetration of moxifloxacin is due to the inherent characteristics of the moxifloxacin molecule, and is not due to changes in the corneal epithelial intercellular (gap) junctions.

**Key Words:** antibiotics/antifungals/antiparasitics • anterior segment • drug toxicity/drug effects

## Appendix B

**TABLE B1**

**Ex-Vivo Corneal Perfusion Chambers  
Fluoroquinolone Comparison  
0.3% Solutions at pH 5.8**

Fluoroquinolone	Rate ( $\mu\text{g}/\text{min}$ )	240 minute Accumulation ( $\mu\text{g}$ )	Lag Time (min)	Permeability Coefficient ( $\times 10^{-7} \text{ cm}/\text{sec}$ )
Moxifloxacin	1.7	325	45	85.2
	1.8	348	51	94.2
Ofloxacin	1.2	246	39	62.6
	1.1	208	48	55.6
Levofloxacin	1.1	210	41	54
	0.91	174	49	46.6

**TABLE B2**

**Ex-Vivo Corneal Perfusion Chambers  
Fluoroquinolone Comparison  
0.5% Solutions at pH 5.8**

Fluoroquinolone	Rate ( $\mu\text{g}/\text{min}$ )	240 minute Accumulation ( $\mu\text{g}$ )	Lag Time (min)	Permeability Coefficient ( $\times 10^{-7} \text{ cm}/\text{sec}$ )
Ofloxacin	2.3	441	48	70.4
	3.1	590	49	94.7
Moxifloxacin	2.4	484	42	75
	2.5	491	44	77
Levofloxacin	1.9	386	42	59.7
	1.6	308	43	47.9



**TABLE B3**

**Ex-Vivo Corneal Perfusion Chambers  
 Fluoroquinolone Comparison  
 0.75% Solutions at pH 5.8**

Fluoroquinolone	Rate ( $\mu\text{g}/\text{min}$ )	240 minute Accumulation ( $\mu\text{g}$ )	Lag Time (min)	Permeability Coefficient ( $\times 10^{-7} \text{ cm}/\text{sec}$ )
Ofloxacin	3.4	667	42	68.6
	3.6	708	46	74.6
Moxifloxacin	3.2	628	44	65.4
	3.6	701	46	74
Levofloxacin	2.9	571	46	60.1
	2.8	528	51	57.1

**TABLE B4**

**Ocular Distribution of Fluoroquinolones  
 After Topical Dosing @ pH 5.8**

Concentration	0.5 %	0.75 %	0.5 %	0.75 %
Fluoroquinolone	Moxifloxacin		Ofloxacin	
Tissue	Concentration ( $\mu\text{g/g}$ or $\mu\text{g/mL}$ ) Mean $\pm$ SE (n = 2)			
Aqueous Humor	1.8 $\pm$ 0.6	3.8 $\pm$ 1.4	1.0 $\pm$ 0.2	1.9 $\pm$ 0.1
Cornea	11 $\pm$ 4	15 $\pm$ 6	9 $\pm$ 3	15.9 $\pm$ 0.1
Upper Palpebral Conjunctiva	0.6 $\pm$ 0.3	2.2 $\pm$ 1.2	1.2 $\pm$ 0.5	2.4 $\pm$ 0.7
Lower Palpebral Conjunctiva	1.5 $\pm$ 0.8	3.6 $\pm$ 1.7	2.1 $\pm$ 1.4	4.0 $\pm$ 0.7
Iris- Ciliary Body	1.1 $\pm$ 0.5	2.5 $\pm$ 1.1	0.9 $\pm$ 0.2	1.7 $\pm$ 0.4